

REMARKS/ARGUMENTS

Upon entry of the present amendments, claims 1, 3-54 and 57 will be pending. Claims 3, 7-9, 21-23, 26, 29 and 33-54 have been withdrawn pursuant to the Restriction Requirement. Claims 2, 55-56 and 58-63 have been canceled without prejudice. Claim 1 has been amended to set forth that the conjugate retains said at least one acid moiety of the negatively charged minor groove binder moiety according to the Examiner's suggestion. Support for this amendment is found on page 2, lines 16-21 and page 35, lines 9-12 of the specification as originally filed. Claim is also amended to set forth that the negatively charged minor groove binder moiety is covalently attached to 3'-position, 5'-position or an internal sugar moiety of said oligonucleotide. Support for this amendment is found in originally filed claim 2. Reconsideration of rejected claims 1, 2, 4-6, 10-20, 24, 25, 27-28, 30-32 and 57 is respectfully requested.

I. Telephone Interview with the Examiner

Applicants wish to thank Examiner Staples for the telephonic interview with Applicants' attorneys William Kezer and Zhe Wu held on November 6, 2008. During the interview, the anticipation and double patenting issues were discussed and proposed amendments for independent claim 1 were presented. Examiner Staples indicated that the amended claims addressed the pending concerns under 35 U.S.C. § 102 (b) and obviousness type double patenting. Applicants thank Examiner Staples for his time and the courtesy of extending the telephonic interview.

II. Inventorship

A. Addition of Alexander A. Gall as a co-inventor

A recently discovered evidence has established that Alexander A. Gall is a co-inventor of the presently claimed invention. In light of this evidence, Applicants submit a request to correct inventorship under 37 C.F.R. §1.48(a) along with the required documents: (i)

statement from additional inventor Alexander A. Gall; (2) substituted Declaration by the actual inventors; (iii) processing fee; and (iv) consent of Assignee.

B. Removal of Sergey Lokhov as an inventor

Applicants respectfully request correction of inventorship and submit herewith a Request under 37 CFR §1.48(b) to remove Sergey Lokhov as an inventor of the subject application as his inventive contribution is no longer being claimed.

C. New Declaration under 37 C.F.R. §1.132 signed by all the inventors

Applicants submit a new Declaration under 37 C.F.R. §1.132, executed by all three co-inventors: Eugeny A. Lukhtanov, Nicolaas M.J. Vermeulen and Alexander A. Gall.

D. Statements by Eugeny A. Lukhtanov and Nicolaas M.J. Vermeulen

Applicants further submit herewith statements by co-inventors Eugeny A. Lukhtanov and Nicolaas M.J. Vermeulen showing the Declaration executed on January 9, 2008 was made without deceptive intent on their part.

III. Rejection of Claims 1, 2, 6, 10, 11, 13, 14, and 57 under 35 U.S.C. § 102(b)

Claims 1, 2, 6, 10, 11, 13, 14, and 57 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Sinyakov et al. (Molecular Biology, 2001, 35, 251-260, hereinafter "Sinyakov"). The Examiner alleges that the minor groove binder MGB-4 described in Figure 2 of Sinyakov anticipates the claimed invention. To the extent that the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. M.P.E.P. § 2131.

Applicants submit that Sinyakov fails to disclose the oligonucleotide-negatively charged minor groove binder conjugate, *wherein the conjugate retains said at least one acidic moiety of the negatively charged minor groove binder moiety*, the feature that is recited in amended claim 1.

Amended claim 1 is directed to an oligonucleotide-negatively charged minor groove binder *conjugate* comprising: a negatively charged minor groove binder moiety comprising: at least one aryl moiety, and at least one *acidic moiety* capable of ionizing under

physiological conditions, wherein said acidic moiety is covalently attached to at least one of said aryl moiety and optionally comprises an acidic moiety linker; an oligonucleotide moiety which is covalently attached to said negatively charged minor groove binder moiety, wherein the conjugate *retains said at least one acidic moiety of the negatively charged* minor groove binder moiety. Therefore, the minor groove binder moiety in the conjugate of the present invention retains at least one acid moiety, which is capable of ionizing to *negatively charged* group.

In contrast, the minor groove binder in the conjugate of Sinyakov fails to *retain* the *acidic moiety* of the negatively charged minor groove binder moiety. The minor groove binder moiety in the conjugate of Sinyakov does *not* contain any acidic moiety because the carboxylic acid group of the minor groove binder has been *consumed* during the formation of the oligonucleotide-minor groove binder conjugate (see, Figure 3, route (a)). As a result, the minor groove binder moiety in the conjugate of Sinyakov *no longer* has a carboxylic group, which is capable of ionizing to negatively charged group.

Figure 3 of Sinyakov illustrates the formation of the conjugate of oligonucleotide HIV-T and minor groove binder MGB-4. The carboxylic acid group on MGB-4 is first converted into a succinimide ester and subsequently *used up* in coupling with the oligonucleotide HIV-T to form the conjugate (see, Figure 3, route (a)). Consequently, the MGB-4 moiety in the conjugate does *not* have any ionizable carboxylic acid group (see, Figure 3). Therefore, Sinyakov fails to teach an oligonucleotide-minor groove binder *conjugate*, wherein *the conjugate retains the at least one acidic moiety of the negatively charged* minor groove binder moiety, the feature that is set forth in the claimed invention. Accordingly, Applicants respectfully request that the rejection of claims 1, 2, 6, 10, 11, 13, 14, and 57 under 35 U.S.C. § 102(b) over Sinyakov be withdrawn.

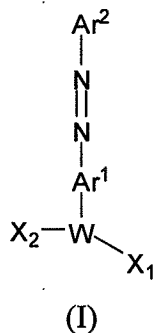
IV. Double Patenting

Claims 1, 2, 4-6, 10-20, 24, 25, 27-28, 30-32 and 57 have been rejected under the judicially created doctrine of obviousness type double patenting as being allegedly unpatentable over claims 1-34 of U.S. Patent No. 6,790,945. To the extent that the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

As set forth in MPEP §804: In determining whether a nonstatutory basis exists for a double patenting rejection, the question to ask is whether the invention defined in a claim in the application would have been anticipated by, or an obvious variation of the invention defined in a claim in a patent. *In re Berg*, 46 USPQ2d 1226 (Fed. Cir. 1998).

Applicants submit that claims 1-34 of U.S. Patent No. 6,790,945 ("the '945 patent") do not anticipate or render amended claim 1 obvious. As stated in Section III above, amended claim 1 is directed to an oligonucleotide-negatively charged minor groove binder conjugate comprising: a negatively charged minor groove binder moiety comprising: at least one aryl moiety, and at least one acidic moiety capable of ionizing under physiological conditions, wherein said acidic moiety is covalently attached to at least one of said aryl moiety and optionally comprises an acidic moiety linker; an oligonucleotide moiety which is covalently attached to said negatively charged minor groove binder moiety, wherein the conjugate *retains* said at least one acidic moiety of the negatively charged minor groove binder moiety and wherein *said negatively charged minor groove binder moiety is covalently attached to 3'-position, 5'-position or an internal sugar moiety of said oligonucleotide*.

In contrast, claims 1-34 of the '945 patent recite an aryl azo phosphoramidite compound having formula (I):



wherein Ar¹ and Ar² are each independently a substituted or unsubstituted aryl group, where at least one of Ar¹ and Ar² is a substituted aryl; X₁ is selected from the group consisting of OH, O-dimethoxytrityl, O-methoxytrityl, O-trityl and an oxygen atom having an acid labile blocking group; X₂ is a phosphoramidite; and W is a linking group having from 3 to 100 backbone atoms selected from C, N, O, S, Si and P, said linking group being cyclic, acyclic,

aromatic or a combination thereof. The compounds of formula (I) is known as a quencher reagent (see, column 7, lines 1-12 of the '945 patent). Clearly, the azo aryl phosphoramidite compounds of formula (I) are structurally *very different* from the oligonucleotide-negatively charged minor groove binder conjugate of the claimed invention. Nowhere does the compounds of formula (I) above disclose or suggest an oligonucleotide-negatively charged minor groove binder *conjugate*, wherein *said negatively charged minor groove binder moiety is covalently attached to 3'-position, 5'-position or an internal sugar moiety of said oligonucleotide*, the features that are recited in the claimed invention. Therefore, the compounds of formula (I) do not anticipate or render the instant claims obvious.

In the Advisory Action, the Examiner states "[t]he patent allows for substituted groups on Ar₁ and Ar₂ and thus allows substituted negatively charged moieties as disclosed in the patent." Applicants respectfully disagree. Applicants direct the Examiner's attention to column 12, line 65 bridging to column 13, line 10 of the '945 patent, wherein the substituents for aryl groups, such as Ar₁ and Ar₂ are defined. None of the aryl substituents defined in the specification can be a negatively charged minor groove binder of the claimed invention. In fact, nowhere does the '945 patent teach or suggest a *negatively charged* minor groove binder moiety. As such, claims 1-34 of the '945 patent do not anticipate or render the instant claims obvious. Accordingly, Applicants respectfully request that the double patenting rejection of 1, 2, 4-6, 10-20, 24, 25, 27-28, 30-32 and 57 be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Appl. No. 10/507,267
Amdt. dated February 23, 2009
Reply to Office Action of October 23, 2008

PATENT

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



Zhe Wu
Reg. No. 52,377

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 925-472-5000
Fax: 415-576-0300
Attachments
Z1W:daw
61692934 v1